

Amendments

In the Claims:

Please substitute pending claims 3-13, 16-24, 29-31 and 33-37 with the following claims 3-13, 16-24, 29-31 and 33-37:

3. (Once amended) Method according to claim 1, characterized in that the prokaryotic cell is *E. coli*.
4. (Once amended) Method according to claim 1, characterized in that the following steps are carried out:
- a) the DNA encoding the tPA, tPA variant, K2S molecule or K2S variant is amplified by PCR;
 - b) the PCR product is purified;
 - c) said PCR product is inserted into a vector comprising the DNA coding for OmpA signal peptide and the DNA coding for gpIII in such a way that said PCR product is operably linked upstream to the DNA coding for the OmpA signal sequence and linked downstream to the DNA coding for gpIII of said vector;
 - d) that a stop codon is inserted between said tPA, tPA variant, K2S molecule or K2S variant and gpIII;
 - e) said vector is expressed by the prokaryotic cell;
 - f) the tPA, tPA variant, K2S molecule or K2S variant is purified.
5. (Once amended) Method according to claim 1, characterized in that the vector is a phagemid vector comprising the DNA coding for OmpA signal peptide and the DNA coding for gpIII.
6. (Once amended) Method according to claim 1, characterised in that the vector is the pComb3HSS phagemid.

7. (Once amended) Method according to claim 1, characterized in that the DNA Sequence of OmpA linked upstream to K2S comprises the following sequence or a functional variant thereof or a variant due to the degenerate nucleotide code:

ATGAAAAAGACAGCTATCGCGATTGCAGTGGCACTGGCTGGTTTCGCTACCG
TGGCCCAGGCAGGCCCTCTGAGGGAAACAGTGACTGCTACTTGGGAATGGGTC
AGCCTACCGTGGCACGCACAGCCTCACCGAGTCGGGTGCCTCCTGCCTCCCG
TGGAATTCCATGATCCTGATAGGCAAGGTTACACAGCACAGAACCCCCAGTG
CCCAGGCACTGGCCTGGCAAACATAATTACTGCCGGAATCCTGATGGGGA
TGCCAAGCCCTGGTGCCACGTGCTGAAGAACCGCAGGCTGACGTGGGAGTA
CTGTGATGTGCCCTCCTGCTCCACCTGCGGCCTGAGACAGTACAGCCAGCCT
CAGTTCGCATCAAAGGAGGGCTTCGCCGACATGCCCTCCCACCCCTGGC
AGGCTGCCATTTGCCAAGCACAGGAGGTGCCCGAGAGCGGTTCCGTG
CGGGGGCATACTCATCAGCTCCTGCTGGATTCTCTGCCGCCACTGCTTCC
AGGAGAGGTTCCGCCACCACCTGACGGTGTACGAGACAGTACAGCCAGCCT
GGTGGTCCCTGGCGAGGAGGAGCAGAAATTGAAGTCGAAAAATACATTGT
CCATAAGGAATTGATGATGACACTTACGACAATGACATTGCGCTGCTGCAG
CTGAAATCGGATTCGTCCCGCTGTGCCAGGAGAGCAGCGTGGTCCGCAGT
TGTGCCTCCCCCGGCCGACCTGCAGCTGCCGACTGGACGGAGTGTGAGCT
CTCCGGCTACGGCAAGCATGAGGCCTGTCTCCTTCTATTGGAGCGGGCTG
AAGGAGGCTCATGTCAGACTGTACCCATCCAGCCGCTGCACATCACACATT
TACTTAACAGAACAGTCACCGACAACATGCTGTGCTGGAGACACTCGGAG
CGCGGGCCCCCAGGCAAATTGCACGACGCCGCCAGGGCGATTGGAGG
CCCCCTGGTGTCTGAACGATGGCCGCATGACTTGGTGGCATCATCAGC
TGGGGCCTGGCTGTGGACAGAAGGATGTCCGGGTGTGTACACAAAGGTTA
CCAACCTACCTAGACTGGATTGCGTACACATGCGACCG (SEQ ID NO:2)

8. (Once amended) Method according to claim 1, characterized in that the DNA Sequence of OmpA comprises the following sequence:

ATGAAAAAGACAGCTATCGCGATTGCAGTGGCACTGGCTGGTTTCGCTACCG
TGGCCCAGGCAGGCC (SEQ ID NO:3)

9. (Once amended) Method according to claim 1, characterized in that the DNA Sequence of OmpA consists of the following sequence:

ATGAAAAAGACAGCTATCGCGATTGCAGTGGCACTGGCTGGTTCGCTACCG
TGGCCAGGCC (SEQ ID NO:3)

10. (Once amended) Method according to claim 1, characterized in that the DNA of the tPA, tPA variant, K2S molecule or K2S variant is preceded by a lac promoter and/or a ribosomal binding site.

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11. (Once amended) Method according to claim 1, characterised in that the DNA coding for the tPA, tPA variant, K2S molecule or K2S variant is selected from the group of DNA molecules coding for at least 90% of the amino acids 87 - 527, 174 - 527, 180 - 527 or 220 - 527 of the human tissue plasminogen activator protein.

12. (Once amended) Method according to claim 5, characterized in that the DNA Sequence of K2S comprises the following sequence or a functional variant thereof or a variant due to the degenerate nucleotide code:

TCTGAGGGAAACAGTGACTGCTACTTGGGAATGGGTAGCCTACCGTGG
CACGCACAGCCTCACCGAGTCGGTGCCTCCTGCCTCCGTGGAATTCCA
TGATCCTGATAGGCAAGGTTACACAGCACAGAACCCCAGTGCCCAGGC
ACTGGGCCTGGCAAACATAATTACTGCCGGAATCCTGATGGGGATGCC
AAGCCCTGGTGCCACGTGCTGAAGAACCGCAGGCTGACGTGGGAGTACT
GTGATGTGCCCTCCTGCTCCACCTGCGGCTGAGACAGTACAGCCAGCCT
CAGTTTCGCATCAAAGGAGGGCTTCGCCGACATGCCCTCCACCCCTG
GCAGGCTGCCATCTTGCCAACCACAGGAGGTGCCCCGGAGAGCGGTTTC
CTGTGCGGGGGCATACTCATCAGCTCCTGCTGGATTCTCTGCCGCCA
CTGCTTCCAGGAGAGGTTCCGCCACCACCTGACGGTGATCTGGGCA
GAACATACCGGGTGGTCCCTGGCGAGGAGGAGCAGAAATTGAAGTCGA
AAAATACATTGTCCATAAGGAATTGATGACACTTACGACAATGACA
TTGCGCTGCTGCAGCTGAAATCGGATTGCTCCGCTGTGCCAGGAGAGC

AGCGTGGTCCGCACTGTGTGCCTTCCCCGGCGGACCTGCAGCTGCCGGA
CTGGACGGAGTGTGAGCTCTCCGGCTACGGCAAGCATGAGGCCTGTCTC
CTTTCTATTGGAGCGGCTGAAGGAGGCTATGTCAGACTGTACCCATCC
AGCCGCTGCACATCACAAACATTACTTAACAGAACAGTCACCGACAACA
TGCTGTGTGCTGGAGACACTCGGAGCGGCGGGCCCCAGGCAAACATTGCA
CGACGCCTGCCAGGGCGATTGGGAGGCCCCCTGGTGTGTGAACGAT
GGCCGCATGACTTGGTGGGCATCATCAGCTGGGCCTGGCTGTGGAC
AGAAGGATGTCCCAGGGTGTGTACACAAAGGTTACCAACTACCTAGACTG
GATTCGTGACAACATGCGACCGTGA (SEQ ID NO:4).

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13. (Once amended) Method according to claim 5, characterized in that the DNA Sequence of K2S consists of the following sequence:

TCTGAGGGAAACAGTGACTGCTACTTGGGAATGGGTAGCCTACCGTGG
CACGCACAGCCTCACCGAGTCGGGTGCCTCCTGCCTCCGTGGAATTCCA
TGATCCTGATAGGCAAGGTTACACAGCACAGAACCCCCAGTGCCAGGC
ACTGGGCCTGGCAAACATAATTACTGCCGGAATCCTGATGGGGATGCC
AAGCCCTGGTGCACGTGCTGAAGAACCGCAGGCTGACGTGGAGTACT
GTGATGTGCCCTCCTGCTCCACCTGCGGCCTGAGACAGTACAGCCAGCCT
CAGTTCGCATCAAAGGAGGGCTTCGCCACATGCCCTCCACCCCTG
GCAGGCTGCCATCTTGCCAAGCACAGGAGGTGCCCCGGAGAGCGGTT
CTGTGCGGGGGCATACTCATCAGCTCCTGCTGGATTCTCTGCCGCCA
CTGCTTCCAGGAGAGGTTCCGCCACACCTGACGGTGATCTGGCA
GAACATACCGGGTGGTCCCTGGCGAGGAGGAGCAGAAATTGAAGTCGA
AAAATACATTGTCCATAAGGAATTGATGATGACACTACGACAATGACA
TTGCGCTGCTGCACTGAAATCGGATTGCTCCGCTGTGCCAGGAGAGC
AGCGTGGTCCGCACTGTGTGCCTTCCCCGGCGGACCTGCAGCTGCCGGA
CTGGACGGAGTGTGAGCTCTCCGGCTACGGCAAGCATGAGGCCTGTCTC
CTTTCTATTGGAGCGGCTGAAGGAGGCTATGTCAGACTGTACCCATCC
AGCCGCTGCACATCACAAACATTACTTAACAGAACAGTCACCGACAACA
TGCTGTGTGCTGGAGACACTCGGAGCGGCGGGCCCCAGGCAAACATTGCA

Q1 CGACGCCTGCCAGGGCGATTGGGAGGCCCCCTGGTGTCTGAACGAT
GCCGCATGACTTGGTGGGCATCATCAGCTGGGCCTGGCTGTGGAC
AGAAGGATGTCCGGTGTGTACACAAAGGTTACCAACTACCTAGACTG
GATTGCGACAACTGCGACCGTG (SEQ ID NO:4).

Concluded
A2 16. (Once amended) DNA molecule according to claim 14, characterized in that said DNA sequence consists of the following sequence:

ATGAAAAAGACAGCTATCGCGATTGCAGTGGCACTGGCTGGTTTCGCTACCG
TGGCCCAGGCAGGCCTCTGAGGGAAACAGTGACTGCTACTTGGGAATGGGTC
AGCCTACCGTGGCACGCACAGCCTCACCGAGTCGGTGCCTCCTGCCTCCCG
TGGAATTCCATGATCCTGATAGGCAAGGTTACACAGCACAGAACCCAGTG
CCCAGGCAGTGGCCTGGCAAACATAATTACTGCCGGAATCCTGATGGGGA
TGCCAAGCCCTGGTGCCACGTGCTGAAGAACCGCAGGCTGACGTGGAGTA
CTGTGATGTGCCCTCCTGCTCCACCTGCAGGCCTGAGACAGTACAGCCAGCCT
CAGTTCGCATCAAAGGAGGGCTTCTCGCCGACATGCCCTCCCACCCCTGGC
AGGCTGCCATCTTGCCAAGCACAGGAGGTGCCGGAGAGCGGTTCTGT
GCCGGGGCATACTCATCAGCTCCTGCTGGATTCTCTGCGCCCACTGCTT
CCAGGAGAGGTTCCGCCACCACCTGACGGTGTCTGGCAGAACATA
CCGGGTGGTCCCTGGCGAGGAGGAGCAGAAATTGAAGTCGAAAAATACA
TTGTCCATAAGGAATTGATGATGACACTTACGACAATGACATTGCGCTGC
TGCAGCTGAAATCGGATTGCTCCGCTGTGCCAGGAGAGCAGCGTGGTCC
GCACTGTGTGCCTCCCCCGGCGGACCTGCAGCTGCCGGACTGGACGGAGT
GTGAGCTCTCCGGTACGGCAAGCATGAGGCCTGTCTCCTTCTATTGGA
GCGGCTGAAGGAGGCTATGTCAGACTGTACCCATCCAGCCGCTGCACATC
ACAACATTACTAACAGAACAGTCACCGACAACATGCTGTGCTGGAGAC
ACTCGGAGCGGCGGGCCCCAGGCAAACCTGCACGACGCCGCCAGGGCGAT
TCGGGAGGCCCCCTGGTGTCTGAACGATGGCCGCATGACTTGGTGGCA
TCATCAGCTGGGCCTGGCTGTGGACAGAACAGGATGTCCCGGGTGTACAC
AAAGGTTACCAACTACCTAGACTGGATTGCGACAAACATGCGACCG (SEQ ID NO:5).

17. (Once amended) DNA molecule according to claim 14, characterized in that said DNA sequence b) is coding for at least 90% of the amino acids 87 - 527 of the human tissue plasminogen activator protein.

18. (Once amended) DNA molecule according to claim 14, characterized in that said DNA sequence b) is coding for at least 90% of the amino acids 174 - 527 of the human tissue plasminogen activator protein.

19. (Once amended) DNA molecule according to any claim 14, characterized in that said DNA sequence b) is coding for at least 90% of the amino acids 180 - 527 of the human tissue plasminogen activator protein.
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20. (Once amended) DNA molecule according to claim 14, characterized in that said DNA sequence b) is coding for at least 90% of the amino acids 220 - 527 of the human tissue plasminogen activator protein.

21. (Once amended) DNA molecule according to claim 14, characterized in that said DNA sequence a) is hybridizing under stringent conditions to the following sequence:
ATGAAAAAGACAGCTATCGCGATTGCAGTGGCACTGGCTGGTTCGCTACCG
TGGCCCAGGCAGGCC (SEQ ID NO:6).

22. (Once amended) DNA molecule according to claim 14, characterized in that said DNA sequence a) consists of the following sequence:
ATGAAAAAGACAGCTATCGCGATTGCAGTGGCACTGGCTGGTTCGCTACCG
TGGCCCAGGCAGGCC (SEQ ID NO:6).

23. (Once amended) DNA molecule according to claim 14, characterized in that said DNA sequence b) is hybridizing under stringent conditions to the following sequence:
TCTGAGGGAAACAGTGACTGCTACTTGGGAATGGGTCAACCTACCGTGGC
ACGCACAGCCTACCGAGTCGGGTGCCTGCCTCCCGTGGATTCCATG

ATCCTGATAGGCAAGGTTACACAGCACAGAACCCCAGTGCCAGGCAGT
GGCCTGGCAAACATAATTACTGCCGAATCCTGATGGGATGCCAAGC
CCTGGTGCCACGTGCTGAAGAACCGCAGGCTGACGTGGAGTACTGTGAT
GTGCCCTCCTGCTCCACCTGCGGCCTGAGACAGTACAGCCAGCCTCAGTT
CGCATCAAAGGAGGGCTTCGCCGACATGCCCTCCACCCCTGGCAGGCT
GCCATCTTGCCAAGCACAGGAGGTGCCCGGAGAGCGGTTCTGTGCGGG
GGCATACTCATCAGCTCCTGCTGGATTCTCTGCCGCCACTGCTTCCAGG
AGAGGTTCCGCCACCACCTGACGGTGATCTGGCAGAACATACCGGG
TGGTCCCTGGCGAGGAGGAGCAGAAATTGAAGTCGAAAAATACATTGTCC
ATAAGGAATTGATGATGACACTTACGACAATGACATTGCGCTGCTGCAGCT
GAAATCGGATTCGTCCCGCTGTGCCAGGAGAGCAGCGTGGTCCGACTGTG
TGCCTCCCCCGCGGACCTGCAGCTGCCGACTGGACGGAGTGTGAGCTCT
CCGGCTACGGCAAGCATGAGGCCCTGTCTCCTTCTATTGGAGCGGCTGAA
GGAGGCTCATGTCAGACTGTACCCATCCAGCCGCTGCACATCACAAACATTAA
CTAACAGAACAGTCACCGACAACATGCTGTGCTGGAGACACTCGGAGCG
GCGGGCCCCAGGCAAATTGCACGACGCCCTGCCAGGGCGATTCGGAGGCC
CCCTGGTGTCTGAACGATGCCGCATGACTTGGTGGCATCATCAGCTG
GGCCTGGCTGGACAGAAGGATGTCCGGGTGTACACAAAGGTTAC
CAACTACCTAGACTGGATTGACAAACATGCGACCGTGA (SEQ ID NO:7).

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24. (Once amended) DNA molecule according to claim 14, characterized in that said DNA sequence b) consists of the following sequence:

TCTGAGGGAAACAGTACTGCTACTTGGGAATGGGTAGCCTACCGTGGC
ACGCACAGCCTACCGAGTCGGGTGCCTCCTGCCCTCCGTGGAATTCCATG
ATCCTGATAGGCAAGGTTACACAGCACAGAACCCCAGTGCCAGGCAGT
GGCCTGGCAAACATAATTACTGCCGAATCCTGATGGGATGCCAAGC
CCTGGTGCCACGTGCTGAAGAACCGCAGGCTGACGTGGAGTACTGTGAT
GTGCCCTCCTGCTCCACCTGCGGCCTGAGACAGTACAGCCAGCCTCAGTT
CGCATCAAAGGAGGGCTTCGCCGACATGCCCTCCACCCCTGGCAGGCT
GCCATCTTGCCAAGCACAGGAGGTGCCCGGAGAGCGGTTCTGTGCGGG

GGCATAACTCATCAGCTCCTGCTGGATTCTCTCTGCCGCCACTGCTCCAGG
AGAGGTTCCGCCACCACCTGACGGTGATCTGGGCAGAACATACCGGG
A2
TGGTCCCTGGCGAGGAGGAGCAGAAATTGAAGTCGAAAAATACATTGTCC
ATAAGGAATTGATGACACTTACGACAATGACATTGCGCTGCTGCAGC
TGAAATCGGATTGTCCTGCTGCCAGGAGAGCAGCGTGGTCCGCACTGT
GTGCCTCCCCGGCGGACCTGCAGCTGCCGGACTGGACGGAGTGTGAGCTC
TCCGGCTACGGCAAGCATGAGGCCTGTCTCCTTCTATTGGAGCGGGCTGA
AGGAGGCTCATGTCAGACTGTACCCATCCAGCCGCTGCACATCACAAACATT
ACTTAACAGAACAGTCACCGACAACATGCTGTGCTGGAGACACTCGGAGC
GGCGGGCCCCAGGCAAATTGCACGACGCCTGCCAGGGCGATTGGAGGC
CCCCTGGTGTCTGAACGATGGCCGCATGACTTGGTGGCATCATCAGCT
GGGCCTGGCTGTGGACAGAAGGATGTCCGGGTGTACACAAAGGTTA
CCAACCTACCTAGACTGGATTGTCGTACAACATGCGACCGTGA (SEQ ID NO:7).

Concluded
29. (Once amended) K2S protein according to claim 27, characterized in that it comprises a protein characterized by the following amino acid sequence or a fragment, a functional variant, an allelic variant, a subunit, a chemical derivative or a glycosylation variant thereof:

A3
SEGNSDCYFGNGSAYRGTHSLTESGASCLPWNSMILIGKVYTAQNPSAQALGLG
KHNCRNPDGDAKPWCHVLKNRRLTWEYCDVPSCSTCGLRQYSQPQFRIKGGL
FADIASHPWQAAIFAKHRRSPGERFLCGGILISSCWILSAAHCFQERFPFHHTVIL
GRTYRVVPGEEQKFEVEKYIVHKEFDDDTYDNDIALLQLKSDSSRCAQESSVV
RTVCLPPADLQLPDWTECELSGYGKHEALSPFYSERLKEAHVRLYPSSRCTSQHL
LNRTVTDNMLCAGDTRSGGPQANLHDACQGDGGPLVCLNDGRMTLVGIISWG
LGCGQKDVPGVYTKVTNYLDWIRDNMRP* (SEQ ID NO:11).

30. (Once amended) K2S according to claim 27, characterized in that it consists of a protein characterized by the following amino acid sequence:

SEGNSDCYFGNGSAYRGTHSLTESGASCLPWNSMILIGKVYTAQNPSAQALGLG
KHNCRNPDGDAKPWCHVLKNRRLTWEYCDVPSCSTCGLRQYSQPQFRIKGGL

a3
FADIASHPWQAAIFAKHRRSPGERFLCGGILISSCWILSAAHCFQERFPPHHTVIL
GRTYRVVPGEQQKFEVEKYIVHKEFDDDTYDNDIALLQLKSDSSRCAQESSVV
RTVCLPPADLQLPDWTECELSGYGKHEALSPFYSERLKEAHVRLYPSSRCTSQHL
LNRTVTDNMLCAGDTRSGGPQANLHDACQGDGGPLVCLNDGRMTLVGIISWG
LGCGQKDVPGVYTKVTNYLDWIRDNMRP* (SEQ ID NO:11).

31. (Once amended) A vector containing a DNA sequence according to claim 14.

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33. (Once amended) The vector pComb3HSS containing a DNA according to claim 14, wherein the expression of the gp III protein is suppressed or inhibited by deleting the DNA molecule encoding said gp III protein or by a stop codon between the gene coding for a polypeptide containing the kringle 2 domain and the serine protease domain of tissue plasminogen activator protein and the protein III gene.

34. (Once amended) A prokaryotic host cell comprising a DNA molecule according to claim 14.

35. (Once amended) A prokaryotic host cell comprising a vector according to claim 31.

36. (Once amended) An *E. coli* host cell comprising a DNA molecule according to claim 14.

37. (Once amended) An *E. coli* host cell comprising a vector according to claim 31.

Please cancel claims 38 and 39.